

ORIGINAL ARTICLE

A Three-Year Retrospective Analysis of the Common Isolated Microorganisms and the Sensitivity Pattern of Blood Culture in Children with Cancer

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Abstract

Background: Cancer patients receiving chemotherapy are facing a higher risk of bloodstream infection (BSI) because of febrile neutropenia. In febrile neutropenia, rational use of antibiotics is important for reducing morbidity and preventing the emergence of drug-resistant bacteria. There is a lack of data on BSI epidemiology in Libyan pediatric cancer patients. We conducted this study to determine the frequency and type of isolated microorganisms, as well as the profile of antibiotic resistance.

Material and methods: This was a three-year retrospective study, 2021-2023. We recorded data on all blood cultures taken from pediatric cancer patients treated at the National Cancer Institute, Misurata, between January 2021 and December 2023. We analyzed the microbiological profile and sensitivity pattern.

Results: The pediatric oncology department sent 615 blood culture samples (168 central venous catheters, 447 peripheral veins) to patients admitted with febrile neutropenia. There were 106/615 (17.6%) positive cultures. Gram-positive organisms were the most commonly isolated bacteria, accounting for 58.2%, and Gram-negative organisms accounted for 37.8%. *Staphylococcus aureus* 56.6% was the most common Gram-positive, and *Pseudomonas aeruginosa* was the most common among Gram-negative bacterium (24/38, 63.15%), followed by *Klebsiella pneumonia* (13/38, 34.2%). A higher proportion of carbapenem resistance isolates were seen in *Klebsiella pneumonia* (10/13, 77%).

Conclusion: The prompt detection of microbial isolates in cancer patients is fundamental to developing an appropriate early treatment policy. The emergence of antibiotic-resistant bacteria is alarming for the use of antibiotics and for institutional infection control protocols.

Keywords: Pediatric cancer, bloodstream infection (BSI), drug-resistance bacteria.

INTRODUCTION

The dramatic development of pediatric cancer therapy, including chemotherapy, radiotherapy, and granulocyte colony-stimulating factor (G-CSF) agents, has a direct effect on improving childhood cancer survival outcomes [1]. Despite these improvements, those patients experienced longer hospitalizations, prolonged chemotherapy-induced immunosuppression, and indwelling catheters, including port-a-cath, central venous line, Hickman line, and urine catheters. Consequently, these factors increase the risk of infection and, in turn, morbidity and mortality [1,2].

The infection could be bacterial, viral, fungal, or protozoa. The bacterial infection is most commonly reported. According to the literature, the incidence of blood-borne infection is around 20% [3]. The literature review indicates that Gram-positive organisms, which account for about 70% of documented infections (Staphylococci and Streptococci), are on the rise, and some of these strains are resistant to methicillin [4,5]. Resistance strains, including vancomycin-resistance and Enterococci, are emerging [6]. The Gram-negative bacteria remain prominent causes of infection. International microbial trends indicate that empirical antibiotics primarily target Gram-positive organisms, while they do not routinely include Gram-negative organisms [7]. Empiric antibiotics routinely administered to all patients with febrile neutropenia include piperacillin/tazobactam plus amikacin. However, most reports of fungal infections refer to them as superinfections, despite the possibility of a primary infection [8,9].

The pattern of microbial infection agents differs from nation to nation and hospital to hospital, depending on local antibiotic stewardship programs and the empirical

antibiotics used [10]. In Libya, a recent study estimating the frequency of causative organisms for nosocomial infections among all age groups reported that Gram-negative bacilli, particularly *E. coli*, and Gram-positive cocci, mainly *Staphylococcus aureus*, were the most isolated pathogens, 24.2%, and 20.4% respectively [11]. There is no previous report among the pediatric cancer group.

This study was conducted to monitor the patterns of microbiological organisms of blood culture and sensitivity reports, and reflect the empirical antibiotics started before the sensitivity report.

MATERIAL AND METHODS

All blood culture samples (multiple cultures per patient) sent from cancer patients at the pediatric oncology department between 1st January 2021 and 3rd December 2023 were retrospectively analyzed. This study was conducted according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement Criteria [12].

We obtained blood culture samples just before initiation of antibiotic treatment and just before the next dose for patients receiving antibiotic treatment outside the hospital. The microbiology laboratory identified the microorganisms found in blood cultures according to the Clinical Laboratory Standards. The microorganisms were isolated, and their antibiotic susceptibilities were specified. Approval was obtained from the local institutional ethical committee board (number: 04/2024). The analysis was conducted using Statistical Package for the Social Sciences (SPSS) 26 software from (SPSS Inc.). Frequencies and percentages were used for the descriptive statistics, and a chi-square test was used to assess the

association between the study variables.

RESULTS

Over three years (2021-2023), 141 children under 16 years with different malignancies presented to the oncology clinic. The mean age was 6.5 years (range: 0.3–16 years) and the male accounts (81/141); the male-to-female ratio was 1.35:1. Solid tumors were the most common [71/141 (50.4%)], consisting of renal tumors [19/71 (26.77%)], brain tumors [15/71 (21%)], Ewing sarcoma [11/71 (15.4%)], neuroblastoma [6/71 (8.4%)], rhabdomyosarcoma [10/71 (14.08%)], germ cell tumors [7/71 (9.8%)], and nasopharyngeal carcinoma [2/71 (2.8%)]. Acute leukemia was [41/141 (29.07%)] a malignancy. Acute lymphoblastic leukemia (ALL) accounted for 36/41 (87.8%), acute myeloid leukemia (AML) accounted for 5/41 (12.2%), and lymphomas accounted for 17/141 (12%), of which 14 were Hodgkin

and 3 were non-Hodgkin. There were [12/141 (8.5%)] rare neoplasms.

During this period, a total of 615 blood cultures were sent. The majority of blood cultures were obtained from patients with acute lymphocytic leukemia [504/615 (82%)]. The frequency of positive culture was [106/615 (17.6%)], and the majority of the samples were from peripheral line sites [447/615 (72.7%)]. The central line site had a higher frequency of positive cultures than the peripheral site, accounting for [47/121 (28%)] and [59/447 (10.3%)] at the central line and peripheral sites, respectively. Bacterial microorganisms were [99/106 (93.3%)] positive cultures, [6/106 (5.6%)] for Candida, and one sample with mixed organisms. A statistically significant association between culture results and the primary tumor and site of blood culture is shown in Table 1.

Table 1: Disease-wise breakdown of bloodstream infection

Variable		Blood culture result		P value
		Positive Frequency (%)	Sterile Frequency (%)	
Diagnosis	Acute lymphocytic leukemia	80 (75.4)	424 (83)	0.026*
	Acute myeloid leukemia	2 (1.8)	13 (86.7)	
	Hodgkin lymphoma	0 (0)	9 (1.7)	
	Solid tumors	24 (22.6)	63 (12.3)	
Site of culture	Central line	47 (44.3)	121(24)	0.0001*
	Peripheral line	59 (55.6)	388 (66)	
Total		106 (17.2)	509 (82.8)	615 (100)
(*) significant p value <0.05				

Gram-positive bacteria accounted for [(61/99) 61.6%], while Gram-negative bacteria accounted for [(38/99) 38.4%]. The most common isolated Gram-positive bacteria were *Staphylococcus spp.* 34/99 (34.3%), within which *S. aureus* (methicillin-sensitive) accounts for 16/34 (47%) and *S. aureus*

(MRSA) [14/34 (41.2%)]. In addition, *Pseudomonas aeruginosa* was the most common among Gram-negative bacteria [24/38 (63.15%)], followed by *Klebsiella pneumoniae* [13/38 (34.2%)]. Isolated microorganism patterns of blood culture are shown in Table 2.

Table 2 presents the isolated microorganisms from blood culture.

Microorganism	Frequency (%)
Gram-positive microorganisms	60 (56.6)
<i>Staphylococcus spp.</i>	34 (34.3)
Coagulase-negative <i>Staphylococcus</i>	3
<i>Staphylococcus aureus</i>	16
MRSA	14
<i>Staphylococcus epidermidis</i>	1
<i>Streptococcus spp.</i>	8 (8.2)
<i>Streptococcus hemolytic</i>	2
<i>Streptococcus non-hemolytic</i>	6
<i>Bacillus spp.</i>	18 (29.5)
Gram-negative microorganisms	38 (35.8)
<i>Klebsiella pneumonia</i>	13 (13.1)
<i>Pseudomonas aeruginosa</i>	24 (24.2)
<i>Acinetobacter</i>	1 (1)
Candida spp.	6 (5.6)
Mixed blood culture	1 (0.9)
Contaminated sample	1 (0.9)
Total	106 (100)

Most Gram-negative organisms were sensitive to colistin (34/38). A higher proportion of carbapenem-resistant Enterobacterales (CRE) isolates was observed in *K. pneumoniae* (10/13, 77%). The six fungal isolates were *Candida albicans*; the sensitivity pattern could not be determined.

The antimicrobial sensitivity profiles

illustrated that the rates of resistance organisms for piperacillin/tazobactam and amikacin were [21/91 22.8%] and [9/88 (10.2%)] respectively. The highest levels of resistance were detected for amoxicillin, trimethoprim-sulfamethoxazole (TMP/SMT), cefotaxim, and ceftriaxone (Table 3).

Table 3: Antimicrobial Sensitivity Profile

Antibiotics		Sensitivity results		
		NA (n)	R (n)	S (n)
Piperacillin/Tazobactam	GNB	2	14	22
	GPB	6	7	48
Amikacin	GNB	1	3	34
	GPB	10	6	48
Imipenem	GNP	2	6	30
	GPB	4	4	53
Meropenem	GNP	2	15	21
	GPB	5	15	41
Amoxicillin	GNB	11	27	0
	GPB	29	20	12

Antibiotics		Sensitivity results		
		NA (n)	R (n)	S (n)
Colistin	GNB	3	0	34
	GPB	-	-	-
Levofloxacin	GNB	14	1	13
	GPB	14	0	16
TMP/SMT	GNB	6	25	6
	GPB	29	16	14
Cefotaxime	GNB	8	28	2
	GPB	27	10	24
Ceftriaxone	GNB	30	7	0
	GPB	35	20	4
Aztreonam	GNB	18	4	13
	GPB	-	-	-

GNB: Gram-negative bacteria; GPB: Gram-positive bacteria; NA: not available; R: resistance; S: sensitive; TMP/SMT: trimethoprim-sulfamethoxazole

DISCUSSION

The immunocompromised status of cancer patients related to disease and chemotherapy-induced neutropenia and mucositis raised the risk for infection. In addition, indwelling catheter-related infections were higher among cancer patients [13-15]. Hematological malignancies have higher rates of morbidity and mortality-related infection compared to solid tumors [16].

In our study of 615 blood cultures, 17.6% of results were positive. The most common causal organisms were the Gram-positive bacteria (61.6%), and *Staphylococcus spp* were most common isolate (34.3%). The methicillin-resistance strain account 41.2% of *S. aureus* bacteria. Similar results by Kipchumba et al, and Daef et al, show that positive bacteria account for around 59% and 53.6% respectively [17,18]. In addition, international trends in the documentation of bacterial infections in Western countries and United States have reported a higher frequency of the Gram-positive bacteria, which is probably due to the increased use of indwelling catheters [4,19,20]. However, the results reported by Turkish, Jordan and Indian studies showed a predominance of

Gram-negative bacteria [13,21-25].

Among the Gram-negative bacteria, *P. aeruginosa* was most frequently detected [24/38 (63.15%)], followed by *K. pneumoniae* [13/38 (34.2%)]. These results closely matched the data reported in the literature [21,22,26]. Our study did not report any instances of *E. coli*-positive cultures. Alarmingly, we found carbapenem-resistant *Enterobacterales* (CRE) isolates of *K. pneumonia* (77%). The reports on the risk factors for CRE in the pediatric age group are limited. Adults and pediatric patients with immunocompromised status are at risk for CRE, but there is no specific risk factor for CRE bloodstream infection (BSI) [27,28].

The antimicrobial sensitivity profiles in our study showed lower resistance rates for piperacillin/tazobactam (22.8%), amikacin (10.2%), and levofloxacin (3%), than previously reported (60%, 36.4%, and 73.7%, respectively) [17]. Nonetheless, the antimicrobial sensitivity results show almost the same rate of resistance to ceftriaxone, amoxicillin, and TMP/SMX [17]. We report that Gram-negative organisms were sensitive to colistin [34/38 (89.4%)], compared to Sampagar et al, who reported a sensitivity

rate of [18/40 (45%)] [23]. In our report, BSI's fungal isolate accounted for 5.6%. In published literature, the frequency of fungal BSI ranges between 2.2% and 14.7% [23,29].

This study was limited by a single-center-based study and retrospective nature. We recommend a larger multi-center prospective approach that includes clinical follow-up and correlation.

In conclusion, the prompt detection of microbial isolates in cancer patients is fundamental to developing an appropriate early policy of treatments. The emergence of antibiotic-resistant bacteria poses a significant concern for the use of antibiotics and institutional infection control protocols.

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Authors Contributions

SMA, NE contributed to the conceptualization and protocol. SMA and NE participated in data collection and revisions. SMA wrote the first draft, conducted the analysis, and wrote the manuscript. All authors proofread the final manuscript and approved it for publication.

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Competing interests

The authors have nothing to declare.

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تحليل بأثر رجعي لمدة ثلاث سنوات للميكروبات الشائعة المعزولة ونمط حساسيتها في مزارع الدم لدى مرضى سرطان الأطفال: تجربة من مركز واحد

سارة محمد الفقيه¹، نواره اغليو²

الملخص

الخلفية: يواجه مرضى السرطان الذين يتلقون العلاج الكيميائي خطرًا متزايدًا للإصابة بعدوى مجرى الدم (BSI) بسبب نقص العدلات الحُموي. في حالات نقص العدلات الحُموي، يُعد الاستخدام الرشيد للمضادات الحيوية أمرًا بالغ الأهمية لتقليل معدلات الاعتلال ومنع ظهور البكتيريا المقاومة للأدوية. هناك نقص في البيانات حول وبائيات عدوى مجرى الدم لدى مرضى سرطان الأطفال في ليبيا. أجرينا هذه الدراسة لتحديد مدى تكرار ونوع الميكروبات المعزولة، بالإضافة إلى نمط مقاومتها للمضادات الحيوية.

المواد والطرق: أُجريت هذه الدراسة بأثر رجعي لمدة ثلاث سنوات، من 2021 إلى 2023. قمنا بتسجيل بيانات جميع مزارع الدم المأخوذة من مرضى سرطان الأطفال الذين عولجوا في المعهد القومي للأورام، مصراته، في الفترة ما بين يناير 2021 وديسمبر 2023. تم تحليل نمط الميكروبيولوجي ونمط الحساسية للمضادات الحيوية.

النتائج: أرسل قسم أورام الأطفال 615 عينة مزرعة دم (168 من قسطة وريدية مركزية، و 447 من أوردة طرفية) لمرضى تم إدخالهم المستشفى بسبب نقص العدلات الحُموي. كانت هناك 615/106 (17.6%) مزرعة إيجابية. كانت الكائنات موجبة الجرام هي البكتيريا الأكثر شيوعًا، حيث شكلت 58.2%، بينما شكلت الكائنات سالبة الجرام 37.8%. كانت المكورات العنقودية الذهبية (*Staphylococcus aureus*) بنسبة 56.6% هي الأكثر شيوعًا بين البكتيريا موجبة الجرام، وكانت الزائفة الزنجارية (*Pseudomonas aeruginosa*) هي الأكثر شيوعًا بين البكتيريا سالبة الجرام (63.15, 38/24)، تليها الكلبسيلا الرئوية (*Klebsiella pneumoniae*) (13/38, 34.2%).

لوحظت نسبة أعلى من العزلات المقاومة للكاربابينيم في الكلبسيلا الرئوية (10/13, 77%).

الخاتمة: يُعد الكشف الفوري عن العزلات الميكروبية لدى مرضى السرطان أمرًا أساسيًا لوضع سياسة علاج مبكر مناسبة. إن ظهور البكتيريا المقاومة للمضادات الحيوية يمثل تحديًا كبيرًا لاستخدام المضادات الحيوية ولبروتوكولات مكافحة العدوى في المؤسسات الصحية.

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